and **treatment**.

AUTHOR: Santago-Borrero P J; Maldonado N; Caceres-Costas M; **Grillo-Lopez A J**

SOURCE: BOLETIN - ASOCIACION MEDICA DE PUERTO RICO, (1971 May) 63 (5) 113-9.
Journal code: AB4. ISSN: 0004-4849.

PUB. COUNTRY: Puerto Rico
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

ENTRY MONTH: 197112

=> fil hom

FILE 'HOME' ENTERED AT 11:59:40 ON 01 FEB 2000

proliferation of B cells activated by anti-IgM, **anti-CD20**, or TPA stimulation, but was not co-stimulatory with B cell growth factor (BCGF), interleukin 1, or interleukin 2. The signal did not depend on the Fc portion of the antibody, because F(ab')2 fragments of anti-Bp50 were also functionally active. Both anti-Bp50 and a low mol. wt. BCGF prepn. were similar in that both were co-stimulatory with the same agents and both anti-Bp50 and BCGF affected activated B cells but not resting B cells. However, a panel of B cell malignancies differed in their responsiveness to anti-Bp50 vs. BCGF: some tumors proliferated in response to anti-Bp50 but not BCGF, whereas other tumors had the opposite pattern. Bp50 had several properties in common with HLA class II mols.: both Bp50 and class II were expressed at lower levels on blood B cells than on tonsillar B cells; the expression of both Bp50 and class II was increased after activation of blood B cells with TPA or anti-IgM; and the expression of both Bp50 and class II was increased after activation of non-T, non-B acute **leukemias** with BCGF. Thus, class II and Bp50 expression may be under common regulatory control.

(FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, SCISEARCH, JICST-EPLUS, CANCERLIT, TOXLIT, TOXLINE' ENTERED AT 11:39:56 ON 01 FEB 2000)

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L15         193 S L11
L16         130 S L12
L17          51 S (L15 OR L16) AND ADMIN?
L18          20 S L17 NOT L9
L19          12 DUP REM L18 (8 DUPLICATES REMOVED)
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L19 ANSWER 1 OF 12 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

```
ACCESSION NUMBER:   1999204427  EMBASE
TITLE:              Fatal cytokine release syndrome with chimeric
                    anti-CD20 monoclonal antibody
                    rituximab in a 71-year-old patient with chronic
                    lymphocytic leukemia [5].
AUTHOR:             Lim L.-C.; Koh L.-P.; Tan P.
CORPORATE SOURCE:   L.-C. Lim, Singapore General Hospital, Singapore,
                    Singapore
SOURCE:             Journal of Clinical Oncology, (1999) 17/6
                    (1962-1963).
                    Refs: 3
                    ISSN: 0732-183X  CODEN: JCONDN
COUNTRY:            United States
DOCUMENT TYPE:      Journal; Letter
FILE SEGMENT:       016     Cancer
                    037     Drug Literature Index
                    038     Adverse Reactions Titles
LANGUAGE:           English
```

L19 ANSWER 2 OF 12 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 2000:44448 BIOSIS
DOCUMENT NUMBER: PREV200000044448
TITLE: Phase I/II study of thrice weekly rituximab in chronic lymphocytic **leukemia** (**CLL**)/small lymphocytic lymphoma (SLL): A feasible and active regimen.
AUTHOR(S): Byrd, John C. (1); Grever, Michael R.; Davis, Brad (1); Lucas, Margaret S.; Park, Kathy (1); Goodrich, Amy (1); Morrison, Candice; Murphy, Timothy (1); Kunkel, Lori; Grillo-Lopez, Antonio; Waselenko, Jamie K. (1); Flinn, Ian W.
CORPORATE SOURCE: (1) Hematology-Oncology Service, Walter Reed Army Medical Center, Washington, DC USA
SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 704a-705a.
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L19 ANSWER 3 OF 12 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999230424 EMBASE
TITLE: Pediatric studies and **hematological malignancies**.
AUTHOR: McKinnon C.
CORPORATE SOURCE: C. McKinnon, Current Drugs Ltd, Middlesex House, 34-42 Cleveland Street, London W1P 6LB, United Kingdom. colinm@cursci.co.uk
SOURCE: IDrugs, (1999) 2/7 (636-638).
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
016 Cancer
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB This report contains some of the more interesting studies presented from the many poster sessions at this year's American Society of Clinical Oncology meeting.

L19 ANSWER 4 OF 12 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1999:525907 SCISEARCH
THE GENUINE ARTICLE: 212CF
Searcher : Shears 308-4994

TITLE: The importance of antibody-specificity in determining successful radioimmunotherapy of B-cell lymphoma

AUTHOR: Illidge T M; Cragg M S; McBride H M; French R R; Glennie M J (Reprint)

CORPORATE SOURCE: SOUTHAMPTON UNIV HOSP, TENOVUS RES LAB, SOUTHAMPTON S016 6YD, HANTS, ENGLAND (Reprint); SOUTHAMPTON UNIV HOSP, TENOVUS RES LAB, SOUTHAMPTON S016 6YD, HANTS, ENGLAND

COUNTRY OF AUTHOR: ENGLAND

SOURCE: BLOOD, (1 JUL 1999) Vol. 94, No. 1, pp. 233-243. Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0006-4971.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 52

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We report the radioimmunotherapy of mouse B-cell lymphoma, BCL1, using a panel of anti-B-cell monoclonal antibodies (MoAb) (anti-CD19, anti-CD22, anti-major histocompatibility complex (MHC) II, and anti-idiotype (Id) radiolabeled with 131-iodine. When **administered** early in disease (day 4), the I-131-anti-MHCII MoAb cured tumors as a result of targeted irradiation alone, the unlabeled MoAb being nontherapeutic. In contrast, I-131-anti-Id, despite targeting irradiation and having therapeutic activity as an unconjugated antibody, protected mice for only 30 days; I-131-anti-CD19 and anti-CD22 were therapeutically inactive. Binding and biodistribution studies showed that the anti-Id, unlike anti-MHCII, MoAb was cleared from target cells in vivo and delivered 4 times less irradiation to splenic tumor. Treating later in the disease (day 14) increased tumor load and produced the expected reduction in therapeutic activity with the anti-MHCII, but surprisingly, allowed I-131-anti-Id to cure most mice. This unexpected potency of I-131-anti-Id late in the disease appeared to result from the direct cytotoxicity of the anti-Id MoAb, which was more active in established disease, in combination with targeted irradiation. We believe the ability of targeted irradiation and certain cytotoxic MoAb to work cooperatively against tumor in this way has important implications for the selection of reagents in radioimmunotherapy of B-cell lymphoma. (C) 1999 by The American Society of Hematology.

L19 ANSWER 5 OF 12 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999141180 EMBASE

TITLE: Acute tumor lysis syndrome: Considerations of cause and prevention.

AUTHOR: Tomera J.F.

CORPORATE SOURCE: Dr. J.F. Tomera, 354 South Street, Medfield, MA 02052-3127, United States
SOURCE: Drugs of Today, (1999) 35/2 (79-87).
Refs: 40
ISSN: 0025-7656 CODEN: MDACAP
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The need for better chemotherapeutic interventional modalities with adjunctive biotherapy and/or immunotherapy to confront oncologic disease processes will continue into the new millennium. Unfortunately, existing problems encountered as a consequence to chemotherapy centering on acute tumor lysis syndrome (ATLS) will also continue. ATLS results when cytotoxic agents lyse, or lacerate, outer plasma membranes of numerous cancerous cells. Eventually, their contents spiel into the bloodstream, indirectly causing kidney damage. This article reviews the induction of ATLS caused by cytotoxic agents and its prevention and/or control. The association of ATLS with the **administration** of chemotherapeutic agents must be considered when treating various types of cancer.

L19 ANSWER 6 OF 12 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999160074 MEDLINE
DOCUMENT NUMBER: 99160074
TITLE: IDEC-C2B8 **anti-CD20** (rituximab) immunotherapy in patients with low-grade non-Hodgkin's lymphoma and lymphoproliferative disorders: evaluation of response on 48 patients.
AUTHOR: Nguyen D T; Amess J A; Doughty H; Hendry L; Diamond L W
CORPORATE SOURCE: Department of Haematology, St Bartholomew's Hospital, London, UK.
SOURCE: EUROPEAN JOURNAL OF HAEMATOLOGY, (1999 Feb) 62 (2) 76-82.
Journal code: ERF. ISSN: 0902-4441.
PUB. COUNTRY: Denmark
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199905
ENTRY WEEK: 19990503

AB This study focused on the efficacy of IDEC-C2B8 (chimeric

anti-CD20) immunotherapy relative to specific subtypes of low-grade lymphoproliferative disorders/non-Hodgkin's lymphomas (LPD/NHL). Forty-eight patients with resistant or relapsed disease completed the IDEC-C2B8 infusion schedule of 375 mg/m2/wk x 4 wk. The LPD/NHL subtypes included: (a) follicular centre cell lymphoma (FCC) in 22 patients; (b) mantle cell lymphoma (MCL) in 10; (c) 1 diffuse large cell lymphoma (DLCL); and (d) the category of small lymphocytic lymphoma/chronic lymphocytic **leukaemia** (SLL/**CLL**) and related disorders in 15 patients. No patient obtained a complete remission. Ten patients (21%) achieved partial remission: 6 FCC, 2 MCL, 1 DLCL and 1 patient from the SLL/**CLL** group. Twenty-eight patients had stable disease and 10 progressed during immunotherapy. In patients with **CLL** and MCL in **leukaemic** phase, there was no correlation between the marked decrease in circulating neoplastic cells following antibody infusions and amelioration of the tumour burden. The results suggest that the subtype of LPD/NHL and the intensity of CD20 on the tumour cells influence the effectiveness of IDEC-C2B8. The antibody was most efficacious against FCC lymphoma. The efficacy (at the dose schedule of 375 mg/m2/wk x 4) against MCL and SLL/**CLL** appeared to be limited, however.

L19 ANSWER 7 OF 12 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998132664 MEDLINE
DOCUMENT NUMBER: 98132664
TITLE: Impact of antigenemia on the bioactivity of infused anti-Tac antibody: implications for dose selection in antibody immunotherapies.
AUTHOR: Junghans R P; Carrasquillo J A; Waldmann T A
CORPORATE SOURCE: Biotherapeutics Development Lab, Harvard Medical School, Division of Hematology-Oncology, Beth Israel Deaconess Medical Center, Boston, MA 02115, USA.. junghans@warren.med.harvard.edu
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Feb 17) 95 (4) 1752-7.
Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199805
ENTRY WEEK: 19980503
AB In patients with malignancies and immune disorders expressing Tac (alpha chain of the interleukin 2 receptor; CD25), physiologic shedding of this receptor may lead to high blood levels of the soluble form (sTac). This system was used to model the interaction of soluble antigen with antibody in therapeutic settings and to develop rational principles to optimize the delivery of antibody to

tumor target cells. First, we confirmed that sTac in vivo can block anti-Tac binding sites and diminish antibody binding to Tac+ cells. Second, the bioactivity of antibody in vivo correlated directly with the amount of antibody infused and inversely with the sTac concentration. Third, bindability of antibody declined in the hours and days after anti-Tac infusion in patients. Finally, tumor targeting was achieved even in the presence of excess sTac, demonstrating a partition of antibody between soluble and cell-bound antigen. A role is proposed for the Brambell receptor (FcRB) to delay saturation of **human** or **chimeric antibodies** via differential catabolism of antigen-antibody complexes. Principles are developed for predicting activity of **administered** antibody in the presence of soluble antigen to assist in dose selection in passive, radioimmuno and immunotoxin therapies.

L19 ANSWER 8 OF 12 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1998:896321 SCISEARCH
THE GENUINE ARTICLE: 140BV
TITLE: Newer treatments for non-Hodgkin's lymphoma: Monoclonal antibodies
AUTHOR: Maloney D G (Reprint); Press O W
CORPORATE SOURCE: FRED HUTCHINSON CANC RES CTR, D1-100, 1100 FAIRVIEW AVE N, POB 19024, SEATTLE, WA 98109 (Reprint); UNIV WASHINGTON, MED CTR, SEATTLE, WA 98195
COUNTRY OF AUTHOR: USA
SOURCE: ONCOLOGY-NEW YORK, (OCT 1998) Vol. 12, No. 10, Supp. [8], pp. 63-76.
Publisher: P R R INC, 17 PROSPECT ST, HUNTINGTON, NY 11743.
ISSN: 0890-9091.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 90

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Significant advances have been made in the application of monoclonal antibody-based therapies to the treatment of patients with lymphoma. The most promising areas appear to be the use of unconjugated monoclonal antibodies and the use of radiolabeled monoclonal antibodies. The recent approval by the US Food and Drug **Administration** (FDA) of rituximab (**Rituxan**), an unconjugated chimeric antibody against the CD20 antigen for the treatment of relapsed low-grade or follicular B-cell non-Hodgkin's lymphoma marked a milestone in the development of these antibody-based treatments. Other new drug applications to the FDA are pending using both unconjugated and radiolabeled monoclonal antibodies, and it is anticipated that further new treatment options based on monoclonal antibody technology will soon be available for

the treatment of patients with non-Hodgkin's lymphoma. Forthcoming clinical trial results combining these new agents with current therapies are needed to determine if the addition of these new biologic agents to our armamentarium against lymphoma will alter the natural history of this disease for our patients. The most promising of these treatments and the comparison of these strategies are reviewed here.

L19 ANSWER 9 OF 12 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 95:237551 SCISEARCH
THE GENUINE ARTICLE: QN128
TITLE: CHARACTERIZATION AND BIODISTRIBUTION OF A MOUSE-**HUMAN CHIMERIC ANTIBODY** -DIRECTED AGAINST PANCREATIC-CANCER MUCIN
AUTHOR: HIRAYAMA K; CHUNG Y S (Reprint); SAWADA T; KIM Y S; SOWA M
CORPORATE SOURCE: OSAKA CITY UNIV, SCH MED, DEPT SURG 1, ABENO KU, 1-5-7 ASAHIMACHI, OSAKA 545, JAPAN (Reprint); OSAKA CITY UNIV, SCH MED, DEPT SURG 1, ABENO KU, OSAKA 545, JAPAN; UNIV CALIF SAN FRANCISCO, VET ADM MED CTR, GASTROINTESTINAL RES LAB, SAN FRANCISCO, CA, 00000
COUNTRY OF AUTHOR: JAPAN; USA
SOURCE: CANCER, (15 MAR 1995) Vol. 75, No. 6, Supp. S, pp. 1545-1553.
ISSN: 0008-543X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 47
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background. Nd2 is a murine monoclonal antibody (MoAb) directed against purified mucins of the human pancreatic cancer cell line SW1990. The authors previously reported promising results with Nd2 for immunotargeting pancreatic cancer. However, murine MoAbs induce human anti-mouse antibodies (HAMAs), a serious problem for clinical use. Mouse/**human chimeric antibodies** may be less immunogenic and therefore reduce the incidence of HAMAs. In this study, the binding affinity, tumor specificity, biodistribution, and immunoimaging of chimeric Nd2 were evaluated.

Methods. The affinity of chimeric Nd2 was evaluated by competition radioimmunoassay and Scatchard analysis using I-125-chimeric Nd2, I-125-murine Nd2, and SW1990 mucin. Immunoreactivity against pancreatic cancer tissues was examined histochemically by the avidin-biotin peroxidase complex method. The biodistribution of the MoAbs was examined in athymic nude mice bearing SW1990 xenografts that were **administered** intravenous I-125-labeled chimeric or murine Nd2. In-111-chimeric Nd2 was injected into the same xenograft models, and scintigrams

were obtained on day 3.

Results. Affinity analysis and immunohistochemical studies showed that chimeric Nd2 had the same affinity to SW1990 mucin and the same specificity for pancreas cancer tissues as murine Nd2. Intravenous **administration** of I-125-chimeric Nd2 resulted in a maximum tumor accumulation of 43% of the initial dose/gram of tumor, which was almost identical to the accumulation of I-125-murine Nd2. Distinct immunoscintigrams of tumors in nude mice were obtained with In-111-chimeric Nd2.

Conclusion. Chimeric Nd2 may have clinical potential in the radioimmunodetection and immunotherapy of pancreatic cancer.

L19 ANSWER 10 OF 12 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 94182058 EMBASE
DOCUMENT NUMBER: 1994182058

TITLE: Myeloablative therapy with autologous bone marrow transplantation as consolidation therapy for recurrent follicular lymphoma.

AUTHOR: Rohatiner A.Z.S.; Johnson P.W.M.; Price C.G.A.; Arnott S.J.; Amess J.A.L.; Norton A.J.; Dorey E.; Adams K.; Whelan J.S.; Matthews J.; MacCallum P.K.; Oza A.M.; Lister T.A.

CORPORATE SOURCE: ICRF Department of Medical Oncology, St. Bartholomew's Hospital,West Smithfield, London EC1A 7BE, United Kingdom

SOURCE: Journal of Clinical Oncology, (1994) 12/6 (1177-1184).
ISSN: 0732-183X CODEN: JCONDN

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purpose: To assess myeloablative therapy with autologous bone marrow transplantation (ABMT) in younger patients with follicular lymphoma in the hope of prolonging remission duration and survival. Patients and Methods: Since June 1985, 64 patients with follicular lymphoma have received cyclophosphamide (CY) 60 mg/kg x 2 and total-body irradiation (TBI) 2 Gy x 6 supported by ABMT as consolidation of second or subsequent remission. The marrow mononuclear cell (MNC) fraction was treated in vitro with three cycles of the monoclonal antibody (MAb) **anti-CD20** and baby rabbit complement before cryopreservation. At the time of treatment, 34 patients were in complete remission (CR), and 30 had residual disease present. Results: The median time to engraftment was 28 days (range, 15 to 46) for both a neutrophil count greater than 0.5 x 109/L and a platelet count greater than 20 x 109/L. Engraftment did

not occur in one patient who died at 12 weeks, and three patients (excluded from the range) have had delayed recovery (> 6 months) of RBCs and platelets. Fifty two patients are alive; three died as a consequence of the transplant procedure, two died in remission from other causes, and seven died of recurrent lymphoma. There was a significant correlation between survival and the total number of episodes of treatment required during the course of the illness (.ltoreq. three v > three, P = .01). With a median follow-up duration of 31/2 years, 35 patients continue in remission between 1 and 8 years, and 24 have developed recurrent lymphoma, five with evidence of transformation to high-grade histology. Freedom from recurrence did not correlate with the time from diagnosis, the number of previous treatments, the presence or absence of residual disease at the time of treatment, or during which specific remission the treatment was given (second v > second). However, comparison with an age-matched, remission-matched, historical control group shows a significant advantage in favor of treatment with CY plus TBI plus ABMT (P = .001); currently, there is no difference in survival. Conclusion: These results are encouraging, although preliminary; it remains to be established whether this treatment prolongs survival.

L19 ANSWER 11 OF 12 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90186614 EMBASE
DOCUMENT NUMBER: 1990186614
TITLE: In vitro and in vivo properties of **human** /mouse **chimeric** monoclonal **antibody** specific for common acute lymphocytic **leukemia** antigen.
AUTHOR: Saga T.; Endo K.; Koizumi M.; Kawamura Y.; Watanabe Y.; Konishi J.; Ueda R.; Nishimura Y.; Yokoyama M.; Watanabe T.
CORPORATE SOURCE: Department of Nuclear Medicine, Kyoto University School of Medicine, 54 Kawahara-cho, Shogoin, Sakyoku, Kyoto 606, Japan
SOURCE: Journal of Nuclear Medicine, (1990) 31/6 (1077-1083). ISSN: 0161-5505 CODEN: JNMEAQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
023 Nuclear Medicine
025 Hematology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A **human**/mouse **chimeric** monoclonal **antibody** specific for a common acute lymphcytic **leukemia** antigen was efficiently obtained by ligating human

heavy-chain enhancer element to the chimeric heavy- and light-chain genes. Cell binding and competitive inhibition assays of both radioiodine and indium-111-(111In) labeled chimeric antiodies demonstrated in vitro immunoreactivity identical with that of the parental murine monoclonal antibodies. The biodistribution of the radiolabeled chimeric antibody in tumor-bearing nude mice was similar to that of the parental murine antibody. Tumor accumulation of radioiodinated parental and chimeric antibodies was lower than thta of 111In-labeled antibodies, probably because of dehalogenation of the radioiodinated antibodies. Indium-111-labeled chimeric antibody clearly visualied xenografted tumor. These results suggest that a **human**/mouse **chimeric antibody** can be labeled with 111In and radioiodine without the loss of its immunoreactivity, and that chimeric antibody localizes in vivo in the same way as the parental murine antibody.

L19 ANSWER 12 OF 12 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 88086398 MEDLINE
DOCUMENT NUMBER: 88086398
TITLE: Suppression of tumor growth by in vivo **administration** of a recombinant **human**-mouse **chimeric** monoclonal **antibody**.
AUTHOR: Yokoyama M; Nishimura Y; Watanabe T
CORPORATE SOURCE: Department of Molecular Immunology, Kyushu University, Fukuoka.
SOURCE: JAPANESE JOURNAL OF CANCER RESEARCH, (1987 Nov) 78 (11) 1251-7.
Journal code: HBA. ISSN: 0910-5050.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198804

AB The in vivo **administration** of a recently described recombinant **human**-mouse **chimeric antibody** specific for a **human** common acute lymphocytic **leukemia** antigen (cALLA) caused significant inhibition of the tumorigenic growth of human **leukemic** cells (Manca cells, expressing cALLA on the surface) which were implanted into nude mice. Intratumor as well as intraperitoneal **administration** of the **human**-mouse **chimeric antibody** repressed the tumor growth of Manca cells in nude mice. In order to investigate the in vivo localization of the antibody molecules, the chimeric antibody was labeled with radioiodine (131I) and injected into nude mice transplanted with Manca cells. The labeled antibody was significantly localized in the tumor and the location of the tumor was successfully visualized by scintiphotoscanning. These results indicated that the recombinant

human-mouse **chimeric antibody** can exert a significant antitumor effect in vivo and can be utilized for radio-immunoimaging. Since the **chimeric human** -mouse monoclonal **antibody** would be expected to have a much lower antigenicity to humans and much higher efficiency in the interaction with **human** effector cells, such recombinant **chimeric antibodies** may be beneficial for immunotherapy and immunoimaging of cancer patients.

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, LIFESCI, SCISEARCH, JICST-EPLUS, CANCERLIT, TOXLIT, TOXLINE' ENTERED AT 11:49:16 ON 01 FEB 2000)

- Author (s)

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L20       10278 S WHITE C?/AU
L21         292 S (GRILLO LOPEZ A? OR LOPEZ GRILLO A?)/AU
L22          98 S L20 AND L21
L23           0 S L22 AND L3
L24           0 S L22 AND L2
L25         112 S (L20 OR L21) AND L2
L26          64 S L25 AND (TREAT? OR THERAP?)
L27          24 DUP REM L26 (40 DUPLICATES REMOVED)

=> d 1-24 ibib abs

L27  ANSWER 1 OF 24  CAPLUS  COPYRIGHT 2000 ACS        DUPLICATE 1
ACCESSION NUMBER:         1999:195380  CAPLUS
DOCUMENT NUMBER:          130:336689
TITLE:                    Rituximab therapy in
                        hematologic malignancy
                          patients with circulating blood tumor cells:
                          Association with increased infusion-related side
                          effects and rapid blood tumor clearance
AUTHOR(S):                Byrd, John C.; Waselenko, Jamie K.; Maneatis,
                          Thomas J.; Murphy, Timothy; Ward, Frank T.;
                          Monahan, Brian P.; Sipe, Melissa A.; Donegan,
                          Sarah; White, Christine A.
CORPORATE SOURCE:         Division of Hematology-Oncology, Walter Reed
                          Army Medical Center, Washington, DC, 20307, USA
SOURCE:                   J. Clin. Oncol. (1999), 17(3), 791-795
                          CODEN: JCONDN; ISSN: 0732-183X
PUBLISHER:                Lippincott Williams & Wilkins
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Purpose: Rituximab was recently approved for use in relapsed,
     low-grade non-Hodgkin's lymphoma; however, few data exist regarding
     the safety of this agent in patients with a high no. of tumor cells
     in the blood.  Methods and Results: After the observation at our
     institution of a rapid redn. of peripheral-blood tumor cells with
     assocd. severe pulmonary infusion-related toxicity in two patients
     with refractory hematol. malignancies, data on
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three addnl. cases were collected from physician-submitted reports of adverse events related to rituximab **treatment**. Five patients with **hematol. malignancies** possessing a high no. of blood tumor cells were **treated** with rituximab and developed rapid tumor clearance. The median age was 68 yr (range, 26 to 78 yr). Patients were diagnosed with B-cell pro-lymphocytic **leukemia** (n = 2), chronic lymphocytic **leukemia** (n = 2), or transformed non-Hodgkin's lymphoma (n = 1). All of these patients had bulky adenopathy or organomegaly. All five patients developed a unique syndrome of severe infusion-related reactions, thrombocytopenia, rapid decrement in circulating tumor cell load, and mild electrolyte evidence of tumor lysis, and all required hospitalization. In addn., one patient developed ascites. These events resolved, and four patients were subsequently **treated** with rituximab without significant complications. Conclusion: Rituximab administration in patients who have a high no. of tumor cells in the blood may have an increased likelihood of severe initial infusion-related reactions. These data also suggest that rituximab may have activity in a variety of other lymphoid neoplasms, such as chronic lymphocytic **leukemia** and B-cell pro-lymphocytic **leukemia**.

L27 ANSWER 2 OF 24 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1999:205437 SCISEARCH
THE GENUINE ARTICLE: 173WY
TITLE: Induction of thioredoxin and thioredoxin reductase gene expression in lungs of newborn primates by oxygen
AUTHOR: Das K C (Reprint); Guo X L; **White C W**
CORPORATE SOURCE: UNIV TEXAS, CTR HLTH, DEPT MOL BIOL, 11937 US HIGHWAY 271, TYLER, TX 75708 (Reprint); NATL JEWISH MED & RES CTR, DEPT PEDIAT, DENVER, CO 80206; UNIV COLORADO, HLTH SCI CTR, DENVER, CO 80262
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY, (MAR 1999) Vol. 20, No. 3, pp. L530-L539.
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 1040-0605.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 50
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Thioredoxin (TRX) is a potent protein disulfide oxidoreductase important in antioxidant defense and regulation of cell growth and signal transduction processes, among them the production of nitric oxide. We report that lung TRX and its reductase, TR, are

specifically upregulated at birth by O-2. Throughout the third trimester, mRNAs for TRX and TR were expressed constitutively at low levels in fetal baboon lungs. However. after premature birth (125 or 140 of 185 days gestation), lung TRX and TR mRNAs increased rapidly with the onset of O-2 or air breathing. Lung TRX mRNA also increased in lungs of term newborns with air breathing. Premature animals (140 days) breathing 100% O-2 develop chronic lung disease within 7-14 days. These animals had greater TRX and TR mRNAs after 1, 6, or 10 days of life than fetal control animals. In 140-day animals given lesser O-2 concentrations (as needed) who do not develop chronic lung disease, lung TRX and TR mRNAs were also increased on days 1 and 6 but not significantly on day 10. In fetal distal lung explant culture, mRNAs for TRX and TR were elevated within 4 h in 95% O-2 relative to 1% O-2, and the response was similar at various gestations. In contrast, TRX protein did not increase in lung explants from premature animals (125 or 140 days) but did in those from near-term (175-day) fetal baboons after exposure to hyperoxia. However, lung TRX protein and activity, as well as TR activity, eventually did increase in vivo in response to hyperoxia (6 days). Increases in TRX and TR mRNAs in response to 95% O-2 also were observed in adult baboon lung explants. When TRX redox status was determined, increased O-2 tension shifted TRX to its oxidized form. **Treatment** of lung explants with actinomycin D inhibited TRX and TR mRNA increases in 95% O-2, indicating transcriptional regulation by O-2. The acute increase in gene expression for both TRX and TR in response to O-2 suggests an important role for these proteins during the transition from relatively anaerobic fetal life to O-2 breathing at birth.

L27 ANSWER 3 OF 24 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 2

ACCESSION NUMBER: 1999297509 EMBASE

TITLE: Rituximab immunotherapy for non-hodgkin's lymphoma.

AUTHOR: **White C.A.**

CORPORATE SOURCE: Dr. C.A. White, Oncology and Hematology, IDEC Pharmaceuticals Corp., San Diego, CA 92121, United States. cwhite@idecpharm.com

SOURCE: Cancer Biotherapy and Radiopharmaceuticals, (1999) 14/4 (241-250).
Refs: 44
ISSN: 1084-9785 CODEN: CBRAFJ

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT:
016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

Searcher : Shears 308-4994

AB In the absence of curative **therapy** for NHL, the objective of **treatment** is to achieve control oft he disease for a meaningful duration and provide relief of tumor-related symptoms without undue toxicity. **Treatment** with Rituximab is a brief, 22-day outpatient **therapy** with limited adverse events in most patients. In clinical studies, 50% of evaluable relapsed or chemotherapy refractory low-grade or follicular NHL patients achieved complete or partial responses. These responses were durable without maintenance **therapy**; the median TIP for responders was 13.2 months and the median duration of response was 11.6 months in the pivotal study. Rituximab is approved as a safe and effective **treatment** for patients with relapsed low- grade or follicular B-cell NHL. It has significant clinical activity, a novel mechanism of action, and compares favorably with alternative **therapies** in response rate and response duration. Completion of ongoing studies will better define the role of alternative Rituximab regimens and Rituximab in the **treatment** of other CD20+ B-lymphocyte malignancies. Radioimmunotherapy with IDEC-Y2B8 may also be added as a **therapeutic** option for NHL patients in the near future.

L27 ANSWER 4 OF 24 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1999:575168 SCISEARCH
THE GENUINE ARTICLE: 218HT
TITLE: Antibody **therapy** with Rituximab for patients with low-grade non-Hodgkin's lymphoma
AUTHOR: Dallaire B K (Reprint); Deardorff J A; **White C A**; Dowden S; Varns C; Shen D; GrilloLopez A J
CORPORATE SOURCE: IDEC PHARMACEUT CORP, 3030 CALLAN RD, SAN DIEGO, CA 92121 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: ONKOLOGIE, (JUN 1999) Vol. 22, No. 3, pp. 184-190. Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND. ISSN: 0378-584X.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 29

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Rituximab (Mabthera(R) Rituxan(R)) is a genetically engineered chimeric murine/human monoclonal antibody directed against the CD20 antigen found on the surface of normal and malignant B lymphocytes; it has recently been licensed in the United States and Europe as a novel antibody **therapy** for patients with relapsed or refractory low-grade or follicular, CD20 positive, B-cell non-Hodgkin's lymphoma (NHL). Preclinical studies have shown that rituximab specifically recognizes the CD20 antigen, can induce human effector mechanisms in vitro, and effectively depletes B cells in

cynomolgus monkeys with limited toxicity. Previous clinical studies have demonstrated that 4 infusions of 375 mg/m(2) rituximab given over a 22-day period in patients with low-grade NHL is effective, with an overall response rate of 50%. Adverse events associated with **treatment** are primarily mild and are most frequent with the first infusion, decreasing with subsequent infusions. B cells are effectively depleted during **treatment**: Levels return to normal ranges between 9 and 12 months post-**treatment**. Immunoglobulin levels of IgM, IgG, and IgA remain within the normal range. A human anti-chimeric antibody response has been detected in only less than 1% of patients **treated** and has not interfered with **treatment**. Rituximab offers a novel, effective, well-tolerated alternative **treatment** for NHL compared with existing **therapies**. The clinic al success of rituximab reinforces the promising potential of a nti body **therapy**.

L27 ANSWER 5 OF 24 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1998:611898 SCISEARCH
THE GENUINE ARTICLE: 107NT
TITLE: Rituximab chimeric Anti-CD20 monoclonal antibody **therapy** for relapsed indolent lymphoma: Half of patients respond to a four-dose **treatment** program
AUTHOR: McLaughlin P (Reprint); GrilloLopez A J; Link B K; Levy R; Czuczman M S; Williams M E; Heyman M R; BenceBruckler I; **White C A**; Cabanillas F; Jain V; Ho A D; Lister J; Wey K; Shen D; Dallaire B K
CORPORATE SOURCE: UNIV TEXAS, MD ANDERSON CANCER CTR, DEPT HEMATOL, 1515 HOLCOMBE BLVD, BOX 68, HOUSTON, TX 77030 (Reprint); IDEC PHARMACEUT CORP, SAN DIEGO, CA; UNIV IOWA, IOWA CITY, IA; STANFORD UNIV HOSP, PALO ALTO, CA; ROSWELL PK CANC INST, BUFFALO, NY; UNIV VIRGINIA, CHARLOTTESVILLE, VA; UNIV MARYLAND, GREENEBAUM CANC CTR, BALTIMORE, MD 21201; OTTAWA GEN HOSP, OTTAWA, ON K1H 8L6, CANADA; TEXAS ONCOL, DALLAS, TX; UNIV SAN DIEGO, MED CTR, SAN DIEGO, CA 92110; UNIV PITTSBURGH, MED CTR, PITTSBURGH, PA
COUNTRY OF AUTHOR: USA; CANADA
SOURCE: JOURNAL OF CLINICAL ONCOLOGY, (AUG 1998) Vol. 16, No. 8, pp. 2825-2833.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0732-183X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 38

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Purpose: The CD20 antigen is expressed on more than 90% of B-cell lymphomas. it is appealing for targeted **therapy**, because it does not shed or modulate. A chimeric monoclonal antibody more effectively mediates host effector functions and is itself less immunogenic than are murine antibodies.

Patients and Methods: This was a multiinstitutional trial of the chimeric anti-CD20 antibody, IDEC-C2B8. Patients with relapsed low grade or follicular lymphoma received on outpatient **treatment** course of IDEC-C2B8 375 mg/m(2) intravenously weekly for four doses.

Results: From 31 centers, 166 patients were entered. Of this intent-to-**treat** group, 48% responded. With a median follow-up duration of 11.8 months, the projected median time ta progression for responders is 13.0 months. Serum antibody levels were sustained longer after the fourth infusion than after the first, and were higher in responders and in patients with lower tumor burden. The majority of adverse events occurred during the first infusion and were grade 1 or 2; fever and chills were the most common events. Only 12% of patients had grade 3 and 3% grade 4 toxicities. A human antichimeric antibody was detected in only one patient.

Conclusion: The response rate of 48% with IDEC-C2B8 is comparable to results with single-agent cytotoxic chemotherapy. Toxicity was mild. Attention needs to be paid to the rate of antibody infusion, with titration according to toxicity. Further investigation of this agent is warranted, including its use in conjunction with standard chemotherapy. J Clin Oncol 16:2825-2833. (C) 1998 by American Society of Clinical Oncology.

L27 ANSWER 6 OF 24 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1998:866929 SCISEARCH
THE GENUINE ARTICLE: 136BP
TITLE: Association of serum Rituximab (IDEC-C2B8) concentration and anti-tumor response in the **treatment** of recurrent low-grade or follicular non-Hodgkin's lymphoma
AUTHOR: Berinstein N L (Reprint); GrilloLopez A J; **White C A**; BenceBruckler I; Maloney D; Czuczman M; Green D; Rosenberg J; McLaughlin P; Shen D
CORPORATE SOURCE: TORONTO SUNNYBROOK REG CANC CTR, DEPT MED, 2075 BAYVIEW AVE, TORONTO, ON M4N 3M5, CANADA (Reprint); TORONTO SUNNYBROOK REG CANC CTR, DEPT IMMUNOL, TORONTO, ON M4N 3M5, CANADA; UNIV TORONTO, TORONTO, ON, CANADA; IDEC PHARMACEUT CORP, SAN DIEGO, CA; OTTAWA GEN HOSP, OTTAWA, ON K1H 8L6, CANADA; FRED HUTCHINSON CANC RES CTR, SEATTLE, WA 98104; ROSWELL PK CANC INST, BUFFALO, NY 14263; US FDA, CTR BIOL

EVALUAT & RES, ROCKVILLE, MD 20857; UNIV TEXAS, MD ANDERSON CANCER CTR, HOUSTON, TX 77030
COUNTRY OF AUTHOR: CANADA; USA
SOURCE: ANNALS OF ONCOLOGY, (SEP 1998) Vol. 9, No. 9, pp. 995-1001.
Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS.
ISSN: 0923-7534.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 27

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background, Monoclonal antibodies are being utilized for **treatment** of patients with low-grade non-Hodgkin's lymphoma as well as other cancers. Results from phase I and II clinical studies has shown that the chimeric monoclonal antibody Rituximab has minimal toxicity and significant **therapeutic** activity in low grade non-Hodgkin's lymphoma.

Patients and methods: We have recently reported on a multicentre pivotal phase III clinical trial involving 166 patients with recurrent low-grade lymphoma who were **treated** with four infusions of Rituximab. Eighty patients (48%) achieved objective responses including 10 patients (6%) with complete responses. Overall, 126 patients (76%) had a greater than or equal to 20% reduction in overall tumor size. The median response duration and time to progression are 11.6 and 13.2 months, respectively. The infusional and long term toxicities were limited.

Results. In this report we describe the pharmacokinetic data obtained on these patients. Measurable concentrations of Rituximab were detected in all patients after the first infusion and increased throughout the **treatment** course. The half-life of the monoclonal antibody increased from 76.3 hours after the first infusion to 205.8 hours after the fourth infusion and was concomitant with a four-fold decrease in the antibody clearance. At three months and six months post-**treatment**, the median Rituximab serum levels were 20.3 mu g/ml (range 0.0 to 96.8 mu g/ml in 104 patients) and 1.3 mu g/ml(range 0.0-28.7 mu g/ml in 13 patients), respectively. A statistically significant correlation was found between the median antibody concentration and response for multiple time points during the **treatment** and followup. The mean serum antibody concentration was also inversely correlated with measurements of tumor bulk and with the number of circulating B cells at baseline.

Conclusions. We conclude that Rituximab is **therapeutically** effective against B-cell lymphoma. Pharmacokinetic data suggests that certain subsets of patients may possibly benefit from increased dosing and studies to address this are currently underway.

L27 ANSWER 7 OF 24 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1999:1001 SCISEARCH
THE GENUINE ARTICLE: 141AW
TITLE: Rituximab **therapy** in **hematologic malignancy** patients with circulating blood tumor cells: Association with increased infusion-related side effects and rapid tumor lysis.
AUTHOR: Byrd J C (Reprint); Waselenko J K; Maneatis T A; Murphy T; Weickum R; Ward F T; **White C A**
CORPORATE SOURCE: WALTER REED ARMY MED CTR, WASHINGTON, DC 20307; BROOKE ARMY MED CTR, SAN ANTONIO, TX; IDEC PHARMACEUT CORP, SAN DIEGO, CA
COUNTRY OF AUTHOR: USA
SOURCE: BLOOD, (15 NOV 1998) Vol. 92, No. 10, Part 1, Supp. [1], pp. 432-432.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0006-4971.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L27 ANSWER 8 OF 24 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:105847 BIOSIS
DOCUMENT NUMBER: PREV199900105847
TITLE: Rituximab **therapy** in **hematologic malignancy** patients with circulating blood tumor cells: Association with increased infusion-related side effects and rapid tumor lysis.
AUTHOR(S): Byrd, J. C.; Waselenko, J. K.; Maneatis, T. A.; Murphy, T.; Weickum, R.; Ward, F. T.; **White, C. A.**
CORPORATE SOURCE: Walter Reed Army Medical Cent., Washington, DC USA
SOURCE: Blood, (Nov. 15, 1998) Vol. 92, No. 10 SUPPL. 1 PART 1-2, pp. 106A.
Meeting Info.: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998 The American Society of Heamatology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L27 ANSWER 9 OF 24 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998111396 MEDLINE
DOCUMENT NUMBER: 98111396
TITLE: Mismatches for two major and one minor

histocompatibility antigen correlate with a patient's rejection of a bone marrow graft from a serologically HLA-identical sibling.

AUTHOR: Lienert-Weidenbach K; Valiante N M; Brown C; **White C**; Johnston-Dow L; McGinnis M; Krausa P; Lakes D M; Wolf J L; Blume K G; Parham P

CORPORATE SOURCE: Department of Structural Biology, Stanford University School of Medicine, CA 94305-5400, USA.

CONTRACT NUMBER: PO1-CA-49605 (NCI)

SOURCE: BIOLOGY OF BLOOD AND MARROW TRANSPLANTATION, (1997 Nov) 3 (5) 255-60.
Journal code: CUA. ISSN: 1083-8791.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199805

ENTRY WEEK: 19980503

AB We describe the case of a patient with chronic myeloid **leukemia** who rejected a bone marrow (BM) graft from a sibling donor believed to be HLA identical. Sequencing of the HLA genes showed the mother to be heterozygous for two closely related HLA haplotypes that could not be resolved by serological typing. The donor and the recipient had each inherited a different maternal haplotype resulting in allelic mismatches for the HLA-B35 and the HLA-DR11 genes. T cell cytotoxicity directed towards the donor's B35 allele was detected in the patient, in addition to CTL specificity for an HLA-B7-restricted minor histocompatibility antigen carried by the donor, resulting in three histocompatibility mismatches between the BM donor and the recipient.

L27 ANSWER 10 OF 24 SCISEARCH COPYRIGHT 2000 ISI (R)

ACCESSION NUMBER: 96:340185 SCISEARCH

THE GENUINE ARTICLE: UH142

TITLE: RADIOIMMUNOTHERAPY OF RELAPSED B-CELL LYMPHOMA WITH YTTRIUM-90 ANTIIDIOTYPE MONOCLONAL-ANTIBODIES

AUTHOR: **WHITE C A (Reprint)**; HALPERN S E; PARKER B A; MILLER R A; HUPF H B; SHAWLER D L; COLLINS H A; ROYSTON I

CORPORATE SOURCE: SIDNEY KIMMEL CANC CTR & SHARP HEALTHCARE, 3099 SCI PK RD, SUITE 200, SAN DIEGO, CA, 92121 (Reprint); UNIV CALIF SAN DIEGO, SAN DIEGO, CA, 92103; VET ADM MED CTR, SAN DIEGO, CA, 92161; IDEC PHARMACEUT CORP, SAN DIEGO, CA, 00000; HYBRITECH INC, SAN DIEGO, CA, 00000

COUNTRY OF AUTHOR: USA

SOURCE: BLOOD, (01 MAY 1996) Vol. 87, No. 9, pp. 3640-3649.
ISSN: 0006-4971.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 34
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Tumor-specific anti-idiotype (anti-Id) monoclonal antibodies (MoAbs) to B-cell lymphomas have been administered to patients, resulting in significant clinical responses. However, clinical responses have been limited by the emergence of Id-negative lymphoma. To overcome the problem of tumor heterogeneity, we conducted a pilot evaluation of the safety and effectiveness of yttrium 90 (Y-90)-labeled anti-Id and shared Id (sId) MoAbs in non-Hodgkin's B-cell lymphoma, Nine patients with relapsed B-cell lymphoma in whom tumor was successfully targeted with In-111-labeled anti-Id MoAb were **treated** with Y-90-labeled anti-id MoAb. A total of 19 courses (one to four per patient) were administered using 1,000 to 2,320 mg unlabeled clearing MoAb and 10 to 54 mCi Y-90 MoAb per patient. Two of nine patients had a complete response, one a partial response, three stable disease, and three disease progression. Time to progression varied from 1 to 12 months. Toxicities were predominately hematologic, and only one patient developed infection and required transfusion, At progression, three of five assessable patients had Id-positive lymphoma and two had Id-negative lymphoma. Human antimouse antibodies (HAMA) did not develop in the patients after **treatment**, Y-90 anti-Id MoAbs demonstrated excellent in vivo stability, produced significantly tumor regression in three of nine patients, exhibited acceptable toxicities, and elicited no HAMA formation, Further investigation of repetitive, low-dose Y-90 anti-Id and MoAb **therapy** is warranted; however, the advantages of a pan B MoAb may prove the latter to be the agent of choice for the radioimmunotherapy of B-cell lymphoma. (C) 1996 by The American Society of Hematology.

L27 ANSWER 11 OF 24 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 92090808 MEDLINE
DOCUMENT NUMBER: 92090808
TITLE: Successful **treatment** of refractory gestational trophoblastic neoplasm with high-dose etoposide and cyclophosphamide.
AUTHOR: Collins R H Jr; **White C S**; Stringer C A; Fay J W
CORPORATE SOURCE: Department of Gynecologic Oncology, Baylor University Medical Center, Dallas, Texas 75246..
SOURCE: GYNECOLOGIC ONCOLOGY, (1991 Dec) 43 (3) 317-9. Journal code: FXC. ISSN: 0090-8258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199204
AB A patient with gestational trophoblastic neoplasm failed **treatment** with several standard chemotherapy regimens and had progressive disease with development of lung and brain metastases and a rising HCG level. Following resection of the metastases and whole-brain radiotherapy she was **treated** with high-dose etoposide and cyclophosphamide. She promptly attained a complete remission and remains free of disease 15 months after completion of **therapy**. This regimen, although initially developed for **leukemia** and lymphoma **treatment**, has potential as a **therapy** for refractory gestational trophoblastic neoplasm because it delivers high doses of agents very active in this disease.

L27 ANSWER 12 OF 24 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 89390864 MEDLINE
DOCUMENT NUMBER: 89390864
TITLE: Survival after isolated cerebral mucormycosis.
AUTHOR: Cook B A; **White C B**; Blaney S M; Bass J W
CORPORATE SOURCE: Department of Pediatric Hematology/Oncology, Triplet Army Medical Center, Honolulu, Hawaii 96859-5000..
SOURCE: AMERICAN JOURNAL OF PEDIATRIC HEMATOLOGY/ONCOLOGY, (1989 Fall) 11 (3) 330-3.
Journal code: 35P. ISSN: 0192-8562.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198912
AB Cerebral mucormycosis is a rare disorder caused by several genera of the family Mucoraceae. The genera Rhizopus, Absidia, and Mucor are the predominant pathogenic groups. Disease caused by these organisms usually complicates an underlying chronic illness, such as diabetes mellitus or malignancy. Cerebral involvement usually occurs from an ascending infection from the paranasal sinuses via the orbit and is usually associated with poorly controlled diabetes. The pulmonary system is the most common site of infection in patients with **leukemia**. Isolated cerebral mucormycosis not associated with head trauma or intravenous drug abuse is a rare disorder. We report what we believe to be the first successfully **treated** case of isolated cerebral mucormycosis in a patient with acute lymphocytic **leukemia** in remission.

L27 ANSWER 13 OF 24 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 90053544 MEDLINE
DOCUMENT NUMBER: 90053544
TITLE: Natural killer lymphocyte blast crisis of chronic myelogenous **leukemia**.
AUTHOR: Warzynski M J; **White C**; Golightly M G;

Steingart R; Otto R N; Podgurski A E; Johnson M L; Glynn P; Smith D E
CORPORATE SOURCE: Immunology Laboratory, Baystate Medical Center, Springfield, Massachusetts 01199..
SOURCE: AMERICAN JOURNAL OF HEMATOLOGY, (1989 Dec) 32 (4) 279-86.
Journal code: 3H4. ISSN: 0361-8609.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199002
AB We describe for the first time a case report documenting a chronic myelogenous **leukemia** (CML) patient who developed a blast crisis of natural killer (NK) lymphocytes. Many of the blasts exhibited large granular lymphocytic (LGL) morphology. Single parameter immunophenotyping results determined that the granulated as well as the agranulated blast cells were NK lymphocytes (CD45, NKH1, CD2, LEU 17, and CD16 positive; CD3, CD8, and LEU 7 negative). Dual parameter flow cytometric testing also determined that some of the blasts expressed the CD11b and CD11c markers as reported for some types of NK lymphocytes. Approximately 10% of the cells were in the S phase of the cell cycle as determined by a modified Vindelov DNA content analysis test and may theoretically reflect some of those cells expressing CD11b and CD11c. The cells did not express in vitro NK lymphocyte functional activity against a K562 target and therefore similar to other reported cases of presumably immature NK lymphocytic **leukemias**. The NK lymphocyte blast crisis was successfully **treated** with vincristine and prednisone. The patient's disease eventually relapsed and transformed to a progenitor stem cell before she died (CD45, 13, CD38, and CD34 positive). The flow cytometric immunophenotyping results contributed significantly as an important adjunct in determining the appropriate diagnosis, helping to select the type of **therapy**, and monitoring the patient with this unusual type of blast crisis.

L27 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 7
ACCESSION NUMBER: 1988:197623 CAPLUS
DOCUMENT NUMBER: 108:197623
TITLE: The pharmacologic basis for the efficacy of high dose ara-C and sequential asparaginase in adult acute myelogenous **leukemia**
AUTHOR(S): Capizzi, Robert L.; **White, Courtland**
CORPORATE SOURCE: Cancer Cent., Wake Forest Univ., Winston-Salem, NC, USA
SOURCE: Yale J. Biol. Med. (1988), 61(1), 11-22
CODEN: YJBMAU; ISSN: 0044-0086
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 39 refs.

L27 ANSWER 15 OF 24 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 88122677 MEDLINE
DOCUMENT NUMBER: 88122677
TITLE: Trimetrexate: clinical development of a nonclassical antifolate.
AUTHOR: O'Dwyer P J; DeLap R J; King S A; **Grillo-Lopez A J**; Hoth D F; Leyland-Jones B
CORPORATE SOURCE: Investigational Drug Branch, National Cancer Institute, Bethesda, MD..
SOURCE: NCI MONOGRAPHS, (1987) (5) 105-9.
Journal code: NS3.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198805
AB Trimetrexate is a 2,4-diaminoquinazoline inhibitor of dihydrofolate reductase (DHFR) which is cytotoxic in vitro and in vivo to several tumors resistant to methotrexate. It is more lipophilic than the parent antifolate, and is not transported by the reduced folate carrier. These features promise activity greater than that of methotrexate in the clinic; its inability to undergo polyglutamylation may also enhance the **therapeutic** index. In preclinical models, the activity of trimetrexate was highly schedule dependent, being superior on repeated dose schedules. Phase I studies have demonstrated that myelosuppression is the major toxic effect of trimetrexate on all schedules tested in man. Phase II studies will evaluate a 5-day schedule initially; trials in multiple tumor types and examination of the role of schedule are already under way.

L27 ANSWER 16 OF 24 TOXLINE
ACCESSION NUMBER: 1988:33600 TOXLINE
DOCUMENT NUMBER: TOXBIB-88-122677
TITLE: Trimetrexate: clinical development of a nonclassical antifolate.
AUTHOR: O'Dwyer P J; DeLap R J; King S A; **Grillo-Lopez A J**; Hoth D F; Leyland-Jones B
CORPORATE SOURCE: Investigational Drug Branch, National Cancer Institute, Bethesda, MD.
SOURCE: NCI MONOGRAPHS, (1987). NCI Monogr, ISS 5, 1987, P105-9.
Journal code: NS3.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: TOXBIB
LANGUAGE: English
OTHER SOURCE: MEDLINE 88122677
Searcher : Shears 308-4994

ENTRY MONTH: 198805

AB Trimetrexate is a 2,4-diaminoquinazoline inhibitor of dihydrofolate reductase (DHFR) which is cytotoxic in vitro and in vivo to several tumors resistant to methotrexate. It is more lipophilic than the parent antifolate, and is not transported by the reduced folate carrier. These features promise activity greater than that of methotrexate in the clinic; its inability to undergo polyglutamylation may also enhance the **therapeutic** index. In preclinical models, the activity of trimetrexate was highly schedule dependent, being superior on repeated dose schedules. Phase I studies have demonstrated that myelosuppression is the major toxic effect of trimetrexate on all schedules tested in man. Phase II studies will evaluate a 5-day schedule initially; trials in multiple tumor types and examination of the role of schedule are already under way.

L27 ANSWER 17 OF 24 MEDLINE DUPLICATE 9

ACCESSION NUMBER: 86226428 MEDLINE

DOCUMENT NUMBER: 86226428

TITLE: Amsacrine-associated cardiotoxicity: an analysis of 82 cases.

AUTHOR: Weiss R B; **Grillo-Lopez A J**; Marsoni S; Posada J G Jr; Hess F; Ross B J

SOURCE: JOURNAL OF CLINICAL ONCOLOGY., (1986 Jun) 4 (6) 918-28.
Journal code: JCO. ISSN: 0732-183X.

PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198609

AB Amsacrine is an antileukemia drug being widely used in North America, Europe, Australia, and New Zealand. In the initial clinical trials, patients **treated** with amsacrine developed occasional instances of acute cardiac arrhythmias and cardiomyopathy. We review and analyze the features of cardiac abnormalities associated with amsacrine in 82 patients, 27 of whom have not been previously reported. The rest have been reported in the literature, but we have included a large amount of additional information about these patients in our analysis. We conclude that amsacrine-related cardiac events are less common than those related to anthracycline chemotherapeutic agents. Manifestations of such toxicity include ECG abnormalities, ventricular and atrial arrhythmias, sudden death, and congestive heart failure. There is little or no cumulative dose effect. Hypokalemia may be a risk factor for development of serious tachyarrhythmias, but such problems can occur despite a normal serum potassium level. Amsacrine appears to affect depolarization and repolarization of the heart,

but the mechanism is unknown.

L27 ANSWER 18 OF 24 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 86277270 MEDLINE
DOCUMENT NUMBER: 86277270
TITLE: CI-921: an analog of amsacrine with experimental activity against solid tumors.
AUTHOR: Grove W R; DeLap L W; **Grillo-Lopez A J**
SOURCE: INVESTIGATIONAL NEW DRUGS, (1986) 4 (2) 113-8.
Journal code: GWJ. ISSN: 0167-6997.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198611
AB CI-921, a 4,5-disubstituted analog of amsacrine, has been selected for clinical testing because of its experimental activity in vitro and in vivo against solid tumors as well as **leukemias**. In studies conducted by Baguley and co-workers, CI-921 demonstrated activity against Lewis lung carcinoma in vivo, producing marked increases in life span and a high proportion of 60-day survivors. An intermittent schedule of administration was more effective than a daily X 5 or daily X 9 schedule. In pharmacokinetic studies in dogs, CI-921 achieved higher plasma concentrations and was cleared more slowly than amsacrine. CI-921 is readily soluble in water and may have antitumor activity when administered orally. Animal toxicology studies indicate that dose-related, reversible leukopenia and thrombocytopenia occur, as well as gastrointestinal toxicity, elevation of alkaline phosphatase and generalized lymphoid depletion. Phase I clinical testing of a parenteral formulation is in progress.

L27 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 11
ACCESSION NUMBER: 1985:613115 CAPLUS
DOCUMENT NUMBER: 103:213115
TITLE: Cytotoxicity of human .beta.-interferon for differentiating **leukemic** HL-60 cells
AUTHOR(S): Hamburger, A. W.; **White, C. P.**; Siebenlist, R. E.; Sedmak, J. J.; Grossberg, S. E.
CORPORATE SOURCE: Cell Culture Dep., Am. Type Cult. Collect., Rockville, MD, 20852, USA
SOURCE: Cancer Res. (1985), 45(11, Pt. 1), 5369-73
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of human interferon (HuIFN) -.alpha. and -.beta. on the proliferation and differentiation induced by DMSO of HL-60 human promyelocytic **leukemia** cells into mature granulocytes was

studied. Neither HuIFN-.alpha. nor -.beta., alone, from 1 to 1000 IU/mL, nor the homologous mock HuIFN prepns. affected HL-60 cell differentiation or proliferation. Although the combination of HuIFN-.alpha. (10 to 1000 IU/mL) with DMSO also did not affect the proliferation or differentiation of HL-60 cells, the addn. of HuIFN-.beta. (1000 IU/mL) and DMSO (1.25%) to growing cultures reduced cell viability as much as 14% of that obsd. for cells **treated** with DMSO alone or to 4% of that obsd. for either untreated cells or those **treated** with HuIFN-.beta. alone. The cytotoxic effect declined with decreasing concns. of HuIFN-.beta.. The cytotoxic effect of DMSO and HuIFN-.beta. was exerted only as cells began to differentiate. Removal of HuIFN-.beta. at day 2 did not reverse the cytotoxic effect, and addn. of HuIFN-.beta. at day 2 did not inhibit cell proliferation. Addn. of HuIFN-.beta. to postmitotic cells on day 4 after DMSO **treatment** did not affect proliferation but did slow differentiation. The cytotoxic and antidifferentiative effects of naturally produced HuIFN-.beta. were confirmed with highly purified recombinant HuIFN-.beta.. Undifferentiated HL-60 cells were resistant to the antiviral effects of HuIFN-.beta., requiring 4 to 6 times the concn. to protect 50% of the cells against vesicular stomatitis virus as that needed to produce a cytotoxic or antidifferentiative effect. The profoundly cytotoxic effects of HuIFN-.beta. reported here may provide a model to study this interferon in combination with inducers of **leukemia** cell differentiation as a possible strategy in cancer **therapy**.

L27 ANSWER 20 OF 24 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 85138499 MEDLINE
DOCUMENT NUMBER: 85138499
TITLE: Neurologic complications of bone marrow transplantation.
AUTHOR: Patchell R A; **White C L 3d**; Clark A W; Beschorner W E; Santos G W
CONTRACT NUMBER: CA-15396 (NCI)
SOURCE: NEUROLOGY, (1985 Mar) 35 (3) 300-6. Journal code: NZ0. ISSN: 0028-3878.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198506
AB Among 78 patients who died after bone marrow transplantation, neurologic complications were present in 55 (70%) and were the cause of death in 5 (6%). Metabolic encephalopathy occurred in 29 patients (37%). CNS infections included aspergillosis (3), herpes simplex encephalitis (2), and Listeria monocytogenes meningitis (1). Six additional patients had neuropathologic changes possibly due to cytomegalovirus infection. Cerebrovascular complications occurred in

five patients (two hemorrhages and three infarcts). All infarcts were associated with endocarditis. The rate of nonbacterial thrombotic endocarditis was significantly higher (p less than 0.001) than in the general autopsy population. CNS **leukemia** and **therapy**-induced injury were rare. There was no evidence of graft-versus-host disease involving the CNS.

L27 ANSWER 21 OF 24 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 84081934 MEDLINE
DOCUMENT NUMBER: 84081934
TITLE: Phase II study of amsacrine gluconate in refractory **leukemia**.
AUTHOR: Omura G A; Winton E F; Vogler W R; Zuckerman K S; **Grillo-Lopez A J**
SOURCE: CANCER TREATMENT REPORTS, (1983 Dec) 67 (12) 1131-2. Journal code: CNM. ISSN: 0361-5960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198404
AB Twenty-six adults with refractory **leukemia** were **treated** with amsacrine gluconate, a new formulation. There were two complete and two partial remissions. This preparation has no apparent advantage when compared with amsacrine lactate.

L27 ANSWER 22 OF 24 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 84142471 EMBASE
DOCUMENT NUMBER: 1984142471
TITLE: Diaziquone (AZQ).
AUTHOR: Bender J.F.; **Grillo-Lopez A.J.**; Posada Jr. J.G.
CORPORATE SOURCE: Warner-Lambert/Parke-Davis Pharmaceutical Research Division, Clinical Oncology Research Program, Ann Arbor, MI 48105, United States
SOURCE: Investigational New Drugs, (1983) 1/1 (71-84). CODEN: INNDDK
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
016 Cancer
038 Adverse Reactions Titles
LANGUAGE: English
AB 1. Diaziquone is an aziridinylbenzoquinone with properties suggestive of an alkylating agent. The drug has shown broad antitumor activity against numerous transplantable murine tumors including curative activity against several intracerebrally implanted tumors. 2. Parent diaziquone appears to have a

t(1/2).beta. of approximately 30 min. The drug is rapidly and widely distributed to tissues as evidence by a t(1/2).alpha. of approximately 1 - 3 min and a volume of distribution exceeding that of total body water. In addition, it rapidly penetrates the central nervous system, reaching peak concentrations (30-50% of corresponding plasma levels) in approximately one hour. Diaziquone is rapidly and extensively metabolized by the liver. 3. Diaziquone is a potent marrow suppressive agent inducing significant degrees of leukopenia, granulocytopenia, and thrombocytopenia in humans. Thrombocytopenia is often severe. Although myelosuppression is for the most part dose related, many patients had significant toxicity even at lower doses. Most investigators have attributed this to the extent of prior **therapy**. Diaziquone demonstrates a very steep dose-response relationship. Myelosuppression was the dose-limiting toxicity in all phase I trials. No nonhematologic dose-limiting toxicity has been identified to date. 4. In phase I and preliminary phase II trials, diaziquone has demonstrated activity against primary brain tumors. Little activity has been seen in other tumor categories. It should be noted, however, that all studies to date have been carried out in heavily pretreated patients. Because of the broad spectrum of antitumor activity in experimental murine tumors, the lack of nonhematologic dose-limiting toxicity, the ability of this drug to attain significant levels in the central nervous system, and the activity of the drug in primary brain tumors, further studies examining its role in the management of patients with cancer are warranted. These studies should be conducted in patients who have had little or no prior **therapy** in order to better evaluate the efficacy of the drug.

L27 ANSWER 23 OF 24 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 72200207 MEDLINE
DOCUMENT NUMBER: 72200207
TITLE: Effect of allopurinol on the pharmacokinetics of 6-mercaptopurine (NSC 755) in cancer patients.
AUTHOR: Coffey J J; **White C A**; Lesk A B; Rogers W I; Serpick A A
SOURCE: CANCER RESEARCH, (1972 Jun) 32 (6) 1283-9. Journal code: CNF. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197210

L27 ANSWER 24 OF 24 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 71282068 MEDLINE
DOCUMENT NUMBER: 71282068
TITLE: Meningeal **leukemia**: challenge in diagnosis